REMARKS

Upon entry of the foregoing amendments, claims 1-9 and 34 will be pending in the application. Claims 1 and 34 are independent claims. Claims 10-33 have been cancelled, without prejudice, as having been withdrawn from consideration by the Examiner and without prejudice to their inclusion in one or more related applications.

Initially, Applicants wish to thank the Examiner for the courteous and productive telephone interview on September 8, 2005, involving the undersigned attorney and Dr. Mark Gibbs, one of the co-inventors, Victor Argaet, Ph.D., Applicants' Australian Patent Attorney, and Christine Hirst, Ph.D., Technology Manager-Biomedical and Health, of The Australian National University, the Assignee of the rights in this application, who was listening to Dr. Gibbs' participation in the interview. During the interview, Dr. Gibbs primarily discussed slides 1 through 11 of a PowerPoint presentation sent to the Examiner by e-mail from the undersigned attorney of September 7, 2005. These slides are directed to an explanation of the present invention as set forth in the present application. Transition slide 12 and slides 13-14 relating to U.S. Patent 5,541,308 of Hogan *et al.* ("Hogan '308") were briefly discussed. Although other slides were included in the PowerPoint presentation sent in the same e-mail mentioned above to Examiner Forman on September 7, they were not discussed in the interview. Instead, after the initial presentation by Dr. Gibbs and discussion of slides 1-14, there was a discussion focusing primarily on claim 1 of the Amendment as presented in an Informal Proposed Amendment forwarded by the undersigned attorney to the Examiner, again by e-mail, on September 8, 2005, just prior to the interview. As a result of the discussions, claims 1 and 34 were amended as set forth in the present Amendment. The substance of the interview is summarized herein.

Support for the foregoing amendments is contained in the application as filed, as follows. Support for an "oligonucleotide array that comprises a set of oligonucleotide probes" is set forth in many locations throughout the application. The term "oligonucleotide array" is defined in paragraph [0063].

Support for the property that the indicated probes discriminate at least one target polynucleotide from a plurality of different polynucleotides is found in many locations

throughout the application. The Examiner's attention is directed to paragraphs [0021], [0023] and [0087], as well as original claims 19 and 22, among other locations.

Support for a target nucleotide having at least one target sequence is supported throughout the application, for example, in paragraphs [0005] and [0010], among many others.

Support for the location of a respective promiscuous probe at an individual address of the oligonucleotide array is also set forth in various locations throughout the application. The Examiner's attention is directed to at least at paragraph [0090], last sentence, paragraph [0119], first sentence, paragraph [0128], last sentence, paragraph [0131] and Fig. 8.

For the foregoing reasons, Applicants respectfully assert that the amendments made herein are fully supported by the specification and do not include new matter. Entry of the amendments is respectfully solicited.

Claim Objections

Claim 8 as presented in the claim listing of the last Amendment filed January 3, 2005, was objected to, as it duplicated claim 9 and was considered a typographical error by the Examiner. The Examiner is correct in that claim 9, rather than claim 8, was inadvertently copied twice and pasted in the last Amendment as claim 8. In the present Amendment, original claim 8, as set forth in the application as filed, is included in the claims listing.

Claim Rejections Under 35 U.S.C. § 102

In Section 3 at pages 2 and 3 of the Office Action, the Examiner took the position that the claims are drawn to a set of oligonucleotide probes described by their function, and concluded that the functions and target descriptions are recitations of intended use for the claimed probes, rather than defining structure or composition of the probes. Applicants respectfully traverse this conclusion.

During the interview, the undersigned attorney explained that the language in the claims, including the clauses mentioned in the Office Action, characterize properties of the set of probes, rather than merely refer to their function or intended use. It is axiomatic that products and their properties are inseparable when interpreting patent claims. That properties of a multi-component product claim may be stated in terms of the interactions among the components was supported by reference to some of the very patents cited by the Examiner and discussed below. Thus, for

example, U.S. Patent 6,306,643 of Gentalen *et al.* ("Gentalen") claims in claim 1 an array comprising a support having regions to which are bound pools of polynucleotide probes where the claim specifically is directed to the binding of various regions among the probes. Similarly, U.S. Patent 6,821,770 of Hogan *et al.* ("Hogan '770") claims in claim 1 a device for detecting nucleic acids comprising, among other things, a plurality of addresses disposed on a solid support where the addresses comprise detectably labeled probes that hybridize certain ribosomal nucleic acids. The claims that were pending even before the present amendments used similar language to Gentalen and Hogan '770 to describe the unique, novel and non-obvious relationship of the probes of the set of probes of the present invention in a way that provides structure to the claimed invention.

Moreover, as a result of the interview, language has been incorporated into independent claims 1 and 34 relating to an oligonucleotide array where, among other claimed properties, a target polynucleotide has at least one target sequence which is related to a respectively promiscuous probe located at an individual address of the oligonucleotide array that hybridizes to a target sequence shared between at least two target nucleotides. In view of the amendments based on the interview, Applicants respectfully submit that the claims specifically and definitively define an oligonucleotide array by virtue of the properties of the components of the array. Accordingly, reconsideration and withdrawal of the conclusion that the claims are defined only by functional language amounting to statements of intended use are respectfully solicited.

U.S. Patent No. 5,541,308 (Hogan '308)

The Examiner rejected claims 1-4, 6 and 34 under 35 U.S.C. § 102(b) as being allegedly anticipated by Hogan '308.

In section 4 of the Office Action, the Examiner alleged that Hogan '308 discloses a set of probes for detecting at least one target polynucleotide (e.g. *Mycobacterium avium)* from a plurality of different targets (Column 12, line 58-Column 13, line 35). Specifically, in her rejection of claims 1 and 34, the Examiner asserted that this reference teaches a set of probes that comprises a collection of different promiscuous probes (*i.e.* genus-specific probes 1-4, Example 8, lines 15-53), wherein the probes are capable of hybridizing to sequences shared by at least two target sequences (*i.e.* Mycobacterium genus), wherein a predefined combination of promiscuous probes hybridizes to at

least two targets and provides specificity of detection (Tables 22-23). Applicants respectfully disagree.

Hogan '308 does not disclose a set of probes at column 12, line 58, to column 13, line 35. A single specific probe is disclosed in column 12, lines 62-67, and column 13, lines 54 and 55.

Hogan '308 discloses a set of probes in Example 8 (columns 27-29) but the statements in this example indicate that the *Mycobacterium* genus is the sole target of those probes. See column 27, lines 22-24 stating:

> ...we have designed probes which detect all members of the genus *Mycobacterium* without crossreacting to the related genera.
> [Emphasis added]

Additionally, columns 12 and 13 and columns 27-29 do not indicate that *Mycobacterium avium* is distinguished from other possible species using promiscuous probes, let alone where a promiscuous probe is located at an individual address of the oligonucleotide array, as presently claimed. *Mycobacterium avium*, the species identified at column 12, is not identified as a target in columns 27 to 29, where the probes disclosed by Hogan '308 are discussed. Additionally, *Mycobacterium avium* is not distinguished (specifically detected) from the other *Mycobacterium* species in Example 8.

Many species from the *Mycobacterium* genus are listed in Table 22 (column 28), but the different species do not represent individual targets or target polynucleotides in Example 8 within the meaning of the instant claims. Further, Hogan '308 makes no statements that indicate different species are individual targets. As the probes are not species-specific, the different species are not distinguished or identified (that is, they are not specifically detected) using the probes defined in this example (column 27).

Columns 27-29 do not indicate that the probes are capable of hybridizing to sequences shared by at least two target polynucleotides, each havingt a target sequence, as they identify only one target, namely the *Mycobacterium* genus.

Hogan '308 does not explicitly or implicitly disclose a specific *Mycobacterium* rRNA gene that comprises at least two target sequences shared with one or more other *Mycobacterium* rRNA genes, and wherein a predefined combination of promiscuous probes, each located at an individual address of an oligonucleotide array, hybridizes to the at least two target sequences of the specific *Mycobacterium* rRNA gene, to thereby provide specificity of detection and

discrimination of that gene. In contrast, Hogan '308 discloses a set of probes that detects all members of the genus *Mycobacterium* rather than detecting specific members of that genus. This conclusion is clearly supported in Hogan '308 at several passages, including the passage quoted above and at column 27, lines 22 to 24.

See also the passage at column 27, lines 39 and 40, which reads:

> The following sequences were characterized and shown to be specific for the genus Mycobacterium. [Emphasis added]

as well as the passage at column 28, lines 9 to 14, which states:

> The results are shown in Table 22 and indicate that the probes hybridize to organisms in the genus *Mycobacterium* and that a combination of probes will detect all members of the genus. Table 23 shows that the probes do not react with other closely related bacteria. [Emphasis added].

Accordingly, if the *Mycobacterium* rRNA genes disclosed in Hogan '308 were construed as being different target polynucleotides, then Hogan '308 does not define a combination of probes that hybridize to at least two targets, as (i) they do not define two targets, and (ii) they do not define any combination of probes that provides specificity of detection or discrimination for a single *Mycobacterium* rRNA gene.

Further, Hogan '308 does not disclose the present inventors' claimed invention including promiscuous probes in individual addresses in different combinations to decrease the number of oligonucleotide probes required for detecting and distinguishing between a plurality of different target polynucleotides. Hogan '308 discloses one target polynucleotide and four probes. Hogan '308 does not disclose a set of probes wherein "a respective promiscuous probe is located at an individual address of the oligonucleotide array and hybridizes to a target sequence shared between at least two of the target polynucleotides, . . . wherein the number of probes in the set is less than the number of target polynucleotides" as claimed in claim 1 and claim 34 of the present application. Further, Hogan '308 does not teach a set of probes in which the number of probes of the set is less than the number of target polynucleotides that are the subject of detection by the set.

Consequently, Hogan '308 fails to disclose each and every one of the elements defined in claims 1 and 34. Since Hogan does not disclose the invention defined by claim 1 for the reasons

mentioned above, Hogan cannot disclose the subject matter of claims 2 through 4 or 6. Accordingly, reconsideration and withdrawal of the anticipation rejection of all of the claims based on Hogan '308 are respectfully solicited.

U.S. Patent No. 6,306,643 (Gentalen)

The Examiner rejected claims 1-4, 6-9 and 34 under 35 U.S.C. § 102(e) as being allegedly anticipated by Gentalen. The Examiner alleged that Gentalen discloses a set of probes for detecting at least one target polynucleotide, the set comprising a collection of different promiscuous probes capable of hybridizing to a target shared between two target polynucleotides (common probe and polymorphic site) wherein a predetermined combination of probes is capable of hybridizing to at least two target sequences providing specificity of detection, citing column 2, line 51-column 3, line 31; column 8, line 45-column 10, line 8, and claim 8. Applicants respectfully traverse this ground of rejection.

The present invention is based on a novel oligonucleotide array in which, among other things, a *decreasing* number of oligonucleotide probes is required for detecting and distinguishing between a plurality of target polynucleotides, and where a promiscuous probe is located at an individual address of the array.

This is in contract to Gentalen, which discloses probe arrays where (a) every probe is present in at least two addresses (spots or features) in the array, and (b) every probe is present in at least one address where it is mixed with one other probe. Thus, Gentalen does not disclose an array wherein a probe is located at an individual address, such that the probe is located at just one address and no other probe is also present at that address. Gentalen uses mixed probes that bind a target cooperatively such that the cooperative binding produces a greater hybridization signal than a signal due to binding of a single probe (see Abstract and column 8, lines 45-65). A mixture of two or more probes is synthesized at one or more spots in every array. Every probe is present in at least one pool and every probe is present in at least two spots in the array (column 2, line 28, to column 4, line 61). Further, this is true of probes that are present but unmixed at a spot (Abstract, column 2, lines 28-42), as every probe that is present unmixed is also present at two or more spots in the array. That is, there is a "pooled" spot and an unmixed spot. Moreover, where probes are reported to be present as unmixed spots, they are used only as controls against which the hybridization signal from the mixed probes is judged (column 9, lines 6-37, and

column 13, line 21-42). Gentalen also teaches the use of more probes (*i.e.*, 4) than the number of alleles to be detected (*i.e.*, 3), rather than less probes than the number of target polynucleotides to be detected, as set forth in the pending claims.

For the foregoing reasons, claims 1 and 34 are novel over Gentalen. Reconsideration and withdrawal of the rejections of claims 1 and 34 are respectfully solicited.

Dependent claims 2-4 and 6-9, by virtue of their dependence on claim 1, must also be novel over Gentalen.

Consequently, Gentalen fails to teach each and every one of the essential elements defined in the pending claims and the Examiner is respectfully urged, therefore, to reconsider and withdraw the rejection of claims 1-4, 6-9 and 34 pursuant to 35 U.S.C. § 102(e).

U.S. Patent 6,821,770 (Hogan '770)

Claims 1-8 and 34 were rejected under 35 U.S.C. § 102(e) as being anticipated by Hogan '770. The Examiner asserted that Hogan '770 discloses a probe set comprising a plurality of promiscuous probes which hybridize to a target shared by at least two targets, and at least one target comprises two sequences shared with others, wherein the number of probes in the set is less than the number of targets and wherein a predefined combination of probe hybridization specifically identifies the targets, citing Example 1 at columns 40-42 and Tables 5-6. Applicants respectfully traverse this rejection.

Example 1 of Hogan '770 does not disclose a set of probes wherein the number of probes in the set is less than the number of target polynucleotides. A set of 41 probes is disclosed in Example 1 to distinguish only five species: *Escherichia coli, Candida albicans, Pseudomonas aeruginosa, Staphylococcus aureus* and *Streptococcus pneumoniae* (see Table 6, rows 4, 26, 42, 47 and 68). None of the other species listed in Table 6 is discriminated. For example, *Bacillus brevis* and *Bacillus subtilis* (rows 1 and 2) produce the same result with positive reactions only to the Pan-Bacterial and Gram (+) probes. The species listed at rows 31-37, rows 57-67 and rows 69-74 also produced positive reactions only to the Pan-Bacterial and Gram (+) probes. Accordingly, none of those species was discriminated. The same is true for every other species listed. Thus, the hybridization reaction produced was the same as the reaction of at least one other species in the list.

In addition, Hogan '770 Example 1 does not disclose a combination of promiscuous probes each located at an individual address of an oligonucleotide array that hybridizes to and provides specificity of detection and discrimination of at least one target polynucleotide. The probe set disclosed in Example 1 of Hogan '770 includes five "species-specific probes" (column 4, lines 58-64, and Table 5), namely, the probes for the species mentioned above. The species-specific probes are not promiscuous, as they do not hybridize to more than one species. The targets specified in the Example are 74 species listed in Table 6, which includes the five previously mentioned species (column 40, line 41, through column 43, line 31, and Table 6). The five species identified in the Example are only discriminated from the 69 undistinguished species by positive reactions with the species-specific probes which are pooled and present in the array, rather than each probe being located at an individual address. Thus, the Hogan '770 probes are present as a mixture, and it is the pattern of hybridization obtained with other probes, for example, the Pan-Bacterial and Gram (+) probes, that allows the five species to be distinguished from each other.

Since Hogan '770 does not disclose an oligonucleotide array having the characteristics set forth in the independent claims 1 and 34 of the present application, this reference cannot anticipate the invention defined by such claims. For the same reasons, Hogan '770 cannot anticipate the invention defined by any of the dependent claims. Reconsideration and withdrawal of the anticipation rejection based on Hogan '770 are respectfully solicited.

Rejection of Claims under 35 U.S.C. § 103

The Examiner maintained the rejection of claim 5 under 35 U.S.C. § 103(a) as being unpatentable over Gentalen in view of Lockhart *et al.* (U.S. Pat. No. 6,329,140) ("Lockhart"). Specifically, the Examiner made the same allegations as those mentioned above in respect of Gentalen but conceded that this reference does not specifically teach a probe set comprising a degenerate probe. The Examiner asserts, however, that Lockhart teaches a similar probe set comprising a degenerate probe wherein the degenerate probe is useful for analyzing polynucleotides encoding polypeptide sequences of interest (column 2, lines 22-44). On this basis, the Examiner concluded that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe sets of Gentalen by including degenerate probes for the asserted expected benefit of analyzing clinically

important polynucleotides and the encoding polypeptide sequences of interest as taught by Lockhart (Column 2, lines 22-44). Applicants respectfully traverse this ground of rejection.

As noted above, Gentalen does not disclose the claimed oligonucleotide array for the reasons set forth above with respect to claims 1 and 34 and thus, the combination with the teachings of Lockhart fails to teach or reasonably suggest each and every one of the elements recited in claim 1, let alone dependent claim 5. Lockhart does not provide the missing elements or any motivation for others to provide them, namely, the property that each promiscuous probe is located at an individual address. Besides, a skilled person would not be motivated to modify the probe set of Gentalen to include a degenerate probe as assertedly taught by Lockhart because Gentalen is primarily concerned with the detection of generic nucleotide polymorphisms, which are sequence specific and which do not relate to or constitute conserved target sequences.

The Examiner also maintained the rejection of claims 5 and 7-9 under 35 U.S.C. § 103(a) as being unpatentable over Hogan '308 in view of Lockhart. The Examiner made the same allegations as those mentioned above in respect of Hogan '308 but admits that Hogan '308 does not specifically teach a probe set comprising a degenerate probe, a high-density array of probes or a linkage via a spacer. It is asserted, however, that Lockhart teaches these missing elements at column 2, lines 22-44, column 28, lines 2-14, and column 12, lines 1-5, and that it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the probe sets of Hogan '308 by including a degenerate probe, a high-density array of probes or a linkage *via* a spacer as taught by Lockhart.

As explained above, however, Hogan '308 does not disclose the claimed oligonucleotide array and thus, even when combined with the teachings of Lockhart, the combination fails to teach or reasonably suggest each and every one of the elements recited in claim 1, let alone claims 5 and 7-9. Moreover, a person of skill in the art would not be motivated to modify the probe set of Hogan '308 to include a degenerate probe as taught by Lockhart because the probe set taught by Hogan '308 already contains probes that hybridize to target sequences conserved between different *Mycobacterium* rRNA genes. At best, the combination of Hogan '308 and Lockhart would motivate a skilled person to use a *Mycobacterium* rRNA genus-specific probe differently in a high-density array or to link it *via* a spacer to a support.

For the foregoing reasons, Applicants respectfully urge the Examiner to reconsider and withdraw the rejection of claims 5 and 7-9 pursuant to 35 USC § 103(a) based on Hogan '308 in view of Lockhart.

Rejection of Claims under 35 U.S.C. § 101 (Double Patenting)

Claims 1-9 remain provisionally rejected under 35 U.S.C. § 101 as claiming the same invention as claims 1-9 of copending Application No. 10/343,170. Application No. 10/343,170 is substantially identical to the present application, but is based on an International PCT Application corresponding to the present application. Applicants will cancel claims 1-9 of Application No. 10/343,170 upon an indication from the Examiner that the pending claims of the present application are otherwise in condition for allowance.

Reconsideration and withdrawal of all objections and rejections and an early indication of allowability of all pending claims are respectfully solicited.

Respectfully submitted,

MARK JOHN GIBBS *et al.*

Sept. 14, 2005

ALAN S. NADEL
Registration No. 27,363
AKIN GUMP STRAUSS HAUER & FELD LLP
One Commerce Square
2005 Market Street, Suite 2200
Philadelphia, PA 19103-7013
Telephone: 215-965-1200
Direct Dial: 215-965-1280
Facsimile: 215-965-1210
E-Mail: anadel@akingump.com

ASN/hg